Single-cell mass cytometry of differential immune and drug responses across a human hematopoietic continuum.

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Public Summary:
Single-cell mass cytometry of differential immune and drug responses across a human hematopoietic continuum. Bendall SC, Simonds EF, Qiu P, El-ad AD, Krutzik PO, Finck R,Bruggner RV, Melamed R Trejo A Ornatsky OI, Balderas RS, Plevritis SK, Sach K, Pe'er D, Tanner SD, and Nolan GP. (2011). Science 332, 687 Flow cytometry is an essential tool for dissecting the functional complexity of hematopoiesis. We used single-cell “mass cytometry” to examine healthy human bone marrow, measuring 34 parameters simultaneously in single cells (binding of 31 antibodies, viability, DNA content, and relative cell size). The signaling behavior of cell subsets spanning a defined hematopoietic hierarchy was monitored with 18 simultaneous markers of functional signaling states perturbed by a set of ex vivo stimuli and inhibitors. The data set allowed for an algorithmically driven assembly of related cell types defined by surface antigen expression, providing a superimposable map of cell signaling responses in combination with drug inhibition. Visualized in this manner, the analysis revealed previously unappreciated instances of both precise signaling responses that were bounded within conventionally defined cell subsets and more continuous phosphorylation responses that crossed cell population boundaries in unexpected manners yet tracked closely with cellular phenotype. Collectively, such single-cell analyses provide system-wide views of immune signaling in healthy human hematopoiesis, against which drug action and disease can be compared for mechanistic studies and pharmacologic intervention.

Scientific Abstract:
Flow cytometry is an essential tool for dissecting the functional complexity of hematopoiesis. We used single-cell "mass cytometry" to examine healthy human bone marrow, measuring 34 parameters simultaneously in single cells (binding of 31 antibodies, viability, DNA content, and relative cell size). The signaling behavior of cell subsets spanning a defined hematopoietic hierarchy was monitored with 18 simultaneous markers of functional signaling states perturbed by a set of ex vivo stimuli and inhibitors. The data set allowed for an algorithmically driven assembly of related cell types defined by surface antigen expression, providing a superimposable map of cell signaling responses in combination with drug inhibition. Visualized in this manner, the analysis revealed previously unappreciated instances of both precise signaling responses that were bounded within conventionally defined cell subsets and more continuous phosphorylation responses that crossed cell population boundaries in unexpected manners yet tracked closely with cellular phenotype. Collectively, such single-cell analyses provide system-wide views of immune signaling in healthy human hematopoiesis, against which drug action and disease can be compared for mechanistic studies and pharmacologic intervention.